1: Hum Immunol 2000 Mar;61(3):279-89

Complementation between specific HLA-DR and HLA-DQ genes in transgenic mice determines susceptibility to experimental autoimmune encephalomyelitis.

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To investigate the contribution of human leukocyte antigen (HLA) class II molecules in susceptibility to inflammatory demyelination, we induced experimental autoimmune encephalomyelitis (EAE) in transgenic (tg) mice expressing the HLA-DR3, HLA-DQ8 and HLA-DQ6 molecules in the absence of endogenous class II (Ab(o)). Following immunization with mouse myelin, HLA-DR3 tg mice mounted strong T-cell proliferative responses, and developed inflammatory lesions and demyelination in the central nervous system with mild to moderate clinical symptoms of EAE. HLA-DQ8 and HLA-DQ6 tg mice elicited weak T-cell proliferative responses and did not develop clinical symptoms of EAE. HLA-DR3/DQ6 double tg mice immunized with mouse myelin experienced clinical disease similar to the single tg HLA-DR3 tg mice, indicating that expression of DQ6 in this line had no effect on disease. In contrast, HLA-DR3/DQ8 double tg mice developed severe inflammatory lesions and clinical disease in response to immunization with mouse myelin. Our data suggest that in the presence of two susceptible class II alleles, namely HLA-DR3 and DQ8, there is additional selection and expansion of potential autoreactive T cells, resulting in enhanced severity of disease.

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Science 253: 1417-1420, 1991

Cell 58: 583-594.

1: Immunol Rev 1999 Dec;172:335-43 Related Articles, Links

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HLA class II transgenic mice: models of the human CD4+ T-cell immune response.

Sonderstrup G, Cope AP, Patel S, Congia M, Hain N, Hall FC, Parry SL, Fugger LH, Michie S, McDevitt HO.

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This review examines the field of current HLA class II transgenic mouse models and the individual approaches applied in production of these mice. The majority of these mice have been created with the objective of obtaining a disease model with clinical features mimicking human autoimmune disease. The development process of a different type of HLA class II transgenic mice, which are designed to function as a substitute for a normal human immune system in studies of human autoantigens, is described. Several HLA-DR4 transgenic lines with normally expressed HLA-DR4 molecules have been produced. To obtain adequate positive selection of the HLA-DR4-restricted CD4+ T-cell repertoire in these mice it is essential both to introduce a human CD4 transgene, and to delete the murine major histocompatibility complex (MHC) class II molecules. These HLA-DR4 transgenic mice have been used to determine the immunogenic CD4+ T-cell epitopes of several human autoantigenic proteins.

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